

REMARKS

Claims 1-19 are hereby been canceled without prejudice to applicants' right to prosecute the canceled claims in a subsequent patent application. Claim 20 is pending in the application and has been examined. Claim 20 stands rejected. New Claims 21-28 have been added. No new matter has been introduced. Applicants respectfully request reconsideration and allowance of Claims 20-28.

Objection to the Specification

The Examiner has objected to the specification on the grounds of its inclusion of an active hyperlink on page 25, line 12. This hyperlink has been deleted, as requested by the Examiner. Applicants respectfully request removal of this ground of objection.

The Rejection of Claim 20 Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claim 20 has been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that lacks an adequate written description in the specification. According to the Examiner, the specification does not provide guidance for the isolation or characterization of DNA from any tree species other than *Pinus taeda*, or for DNA markers other than SSRs from any tree species. Applicants respectfully disagree for the following reasons.

The applicants are not claiming nucleic acid sequences or amino acid sequences *per se*, contrary to the cases cited by the Examiner (*University of California v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) and *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991)). Therefore, the written description requirement may be met without disclosing specific amino acid or nucleic acid sequences.

Second, the Federal Circuit has recently clarified that "[i]t is incorrect . . . that all functional descriptions of genetic material fail to meet the written description." *Enzo Biochem. Inc. v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002). The functional

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characteristics of the DNA used to determine pedigree according to the applicants' invention are well defined in the specification. In short, the DNA molecules must allow the determination or inference of an individual tree's genotype, which is then used to infer the pedigree of the individual tree. Specification, page 12, lines 4-13. One skilled in the art would recognize that the specific identity of the DNA molecules used for determining the pedigree is irrelevant to the applicants' invention. The only knowledge about the DNA that is necessary for the practice of the invention is its effectiveness as a vehicle for establishing pedigree information. For example, a pedigree may be established based on the absence or presence of a particular band or set of bands on a gel (for example, a DNA fingerprint). It is not important to know the nucleic acid sequence associated with that band or set of bands. Thus, one skilled in the art would appreciate that applicants had possession of the claimed invention at the time the application was filed. Accordingly, applicants respectfully request withdrawal of this ground of rejection.

The Rejection of Claim 20 Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claim 20 has been rejected under 35 U.S.C. § 112, first paragraph, for lack of an enabling description in the specification. The Examiner alleges lack of enablement with respect to (1) the identification and isolation of a multitude of markers from a multitude of tree species, (2) the development and evaluation of a progeny scoring system in a multitude of tree species and for a multitude of phenotypes, (3) the use of polymix breeding to obtain selectable phenotype changes in a multitude of tree species for a multitude of traits, and (4) the use of a multitude of DNA markers to identify the pedigree of a multitude of progeny from a multitude of tree species and polymix-generated progeny.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in a patent coupled with information known in the art without undue experimentation. A patent need not teach, and preferably omits, what is well known in the

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art. M.P.E.P. Section 2164.01. Applicants provide evidence below that one of ordinary skill in the art could practice the invention without undue experimentation at the time the application was filed.

The Examiner states that polymix breeding of trees for phenotypic change is unpredictable, given the lack of available knowledge regarding flower biology or pollination control in many tree species, citing White (1996) in *Proc. QFRI-IUFRO Conf. Tree Improvement for Sustainable Tropical Forestry*, Caloundra, Australia, page 113, column 1, second paragraph. Applicants respectfully submit that White neither discloses that polymix breeding of trees for phenotypic change is unpredictable nor that there is a lack of available knowledge regarding flower biology or pollination control. Specifically, White states that "[f]or many tropical species, it seems likely that open-pollination will be an attractive mating design to consider because . . . little *may* be known about flowering biology and pollen handling techniques making control pollination difficult." White, page 113, column 1, second paragraph (emphasis added). Thus, White is merely opining that controlled pollination techniques, such as polymix breeding, may be difficult if little is known about flowering biology and pollen handling techniques. In fact, rather than supporting the unpredictability of polymix breeding of trees, White states that

Half-sib mating designs (including *polymix* and OP families when the OP families approximate half-sib families) are optimal or very nearly optimal over a broad range of conditions for both estimating heritabilities and $g \times e$ and also for ranking parents (and hence maximising gain from backward selection). White, page 111, first column, second paragraph (emphasis added).

According to the Examiner's reasoning, open-pollinated breeding would be even less predictable than polymix breeding given that the potential pollen contributors are not fully known, as they are with polymix breeding. On the contrary, it has been found that open-

pollination breeding gives good estimation of parental breeding values and heritability estimates. Specification, page 3, line 33, to page 4, line 5. Moreover, simulation studies have shown that polymix breeding with no parental analysis can provide genetic gains nearly as good as those achieved using full-sib (full-pedigree) systems. Specification, page 6, lines 10-18.

The Examiner also states that the use of polymix breeding may be confounded by the unequal reproductive success of many parents' pollen, which would lead to incorrect measurements of general recombining ability, citing Rogers & Boyle (1991) *Heredity* 67:373-9 and Moran & Griffin (1985) *Silvae Genet.* 34:117-21. However, equal fertilization success of the pollen parents of the premix is not essential to the success of the methods of the invention. Moreover, contrary to the Examiner's assertion, polymix breeding provides excellent estimation of breeding value and general recombining ability. Specification, page 6, lines 2-7. The applicants recently co-authored a publication (submitted herewith as Attachment A) reviewing studies describing the relative reproductive success of male pollen in mixtures, including the two studies cited by the Examiner. Lambeth et al. (2001) *Theor. Appl. Genet.* 103:930-43, page 939, column 1. Lambeth et al. concluded that even though "most of these studies were done with few (two to six) pollen parents in the mixture, differential paternal parent contributions were slight." Lambeth et al., page 939, column 1. Indeed, Moran & Griffin conclude that, despite evidence of non-random contribution of pollens to viable seed formation, "such effects are not so strong as to affect the utility of the polymix mating design in practical tree breeding." Moran & Griffin, page 121, column 1, last paragraph. In order to reduce the probability that any one pollen parent will dominate in fertilization, Lambeth et al. recommended using several males (>20) in polymix crossing schemes. Lambeth et al. (2001), page 939, column 1. For example, applicants used a pollen premix from 39 parents in an illustrative embodiment of their invention. Specification, page 22, lines 1-3.

The Examiner cites Stoehr et al. to support his argument that environmental effects on trait expression may confound the selection of desirable progeny that possess heritable genetic components conferring the phenotypic change. Stoehr et al. states that "the environment that seeds are produced under has an effect on several germination characteristics, physiological traits, and height growth." Stoehr et al., page 423, column 1. The effects of environmental changes on plant phenotypes have been known for a long time, and one skilled in the art would appreciate the importance of controlled experimentation and would control for environmental influences, for example, by growing each lot of seeds in the same location.

The Examiner further states that molecular marker-mediated selection in tree breeding is unpredictable. Applicants point out that their tree breeding methods do not involve marker-assisted selection. The only use of the molecular markers in the methods of the invention is for parental analysis. The parental analysis used in the methods of the invention allows the determination of the full pedigree of selected progeny and the use of the breeding value of both the male and female to help predict the breeding value of progeny for the next generation of breeding. Thus, the inclusion of parental analysis in the methods of the invention eliminates the loss of inbreeding and pedigree control associated with polymix breeding. Because applicants' invention does not involve the use of molecular marker-mediated selection, the Examiner's arguments are not applicable to the methods of the invention.

According to the Examiner, no guidance is provided (1) for the isolation or characterization of DNA from any tree species other than *Pinus taeda*, (2) for the characterization of DNA markers other than SSRs, (3) for the determinations of phenotypes of progeny trees and for selecting elite trees from the progeny, and (4) for the determination of actual pedigrees. Applicants respectfully disagree.

First, methods for the isolation and characterization of DNA from trees are standard in the art. For example, a wide variety of DNA extraction and purification methods have been developed for preparing DNA samples from a wide variety of plant tissues and different plant species. *See, e.g.*, Specification, page 14, line 34, to page 15, line 2.

Second, the development and use of informative markers for pedigree analyses in a number of species, including trees, is also known in the art. *See, e.g.*, Specification, page 16, lines 1-18. The methods for detecting SSR markers that are described in the specification are equally applicable to the detection of any polymorphic nucleic acid marker (*i.e.*, nucleic acid amplification and assessment of distribution, inheritance, and variability of polymorphic markers). Specification, page 26, line 18, to page 31, line 19.

Third, the determination of plant phenotypes is standard in plant breeding methods. The specification describes examples of plant phenotypic traits that are commonly assayed, as well as methodology to assess the statistical significance of a phenotypic score. Specification, page 13, lines 20-35. Moreover, the specification provides guidance for selecting elite trees from the progeny, for example, at page 16, line 19, to page 17, line 4.

Fourth, the Specification provides guidance for the determination of pedigrees of individual plants. The combination of seven chloroplast and three nuclear microsatellite loci provided a unique fingerprint for each of the 45 selections described in the specification, despite the considerable level of relatedness between the parental trees. Specification, page 31, lines 14-17. Importantly, the specification discusses useful strategies for unambiguously determining pedigree, such as increasing the number of nuclear or chloroplast markers, eliminating related individuals from the breeding populations, or creating polymixes that avoid mixing pollens known to share the same paternal haplotype. Specification, page 18, line 13, to page 20, line 22. Specifically, for the 45 selections described in the specification, it is stated that

the addition of 2-3 more loci "would likely add sufficient discriminating power to unambiguously fingerprint every individual in most pine breeding programs or clonal trials." Specification, page 31, lines 17-19.

Therefore, for the reasons described above, applicants submit that Claim 20, and claims dependent therefrom, are supported by an enabling disclosure. Applicants respectfully request removal of this ground of rejection.

The Rejection of Claim 20 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claim 20 under 35 U.S.C. § 103(a) as being rendered obvious by Bridgwater (1992) in *Handbook of Quantitative Forest Genetics*, Kluwer Academic Pub., Dordrecht, The Netherlands, pages 69-95 in view of El-Kassaby & Ritland (1992) *Theor. Appl. Genet.* 83(6-7):752-8 and Stoechr et al. (1998) *Can. J. For. Res.* 28:187-95. According to the Examiner, it would have been obvious to one of ordinary skill in the art to modify the method of polymix tree breeding taught by Bridgwater by using the pedigree analysis step in the polymix breeding program in El-Kassaby et al. and the DNA markers disclosed by Stoechr et al. Applicants respectfully disagree.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the referenced teachings. In addition, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. M.P.E.P. § 706.02(j). "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." *In re Fritch*, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992); *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1459 (Fed. Cir. 1998) ("even when the level of skill in the art is high, the Board must identify specifically the

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principle, known to one of ordinary skill, that suggests the claimed combination. In other words, the Board must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."); *In re Lee*, 61 U.S.P.Q.2d 1430, 1434 ("The examiner's conclusory statements . . . do not adequately address the issue of motivation to combine. This factual question of motivation is material to patentability, and could not be resolved on subjective belief and unknown authority.").

Bridgwater discloses tree-breeding strategies including polymix breeding. However, Bridgwater neither suggests nor provides any motivation for using a pedigree analysis step in a polymix-breeding program, as required in the claimed method of the invention.

Stoehr et al. used a polymorphic genome marker to evaluate pollen contamination, supplemental mass pollination efficacies, and natural selfing in Douglas fir. However, Stoehr et al. neither suggests nor provides any motivation for using a pedigree and a phenotype score to identify elite trees for use in a next generation of tree breeding, as required in the claimed method of the invention.

El-Kassaby & Ritland used isozyme markers to investigate frequency-dependent male reproductive success in a polycross of Douglas fir. However, El-Kassaby & Ritland neither suggests nor provides any motivation for using a pedigree and a phenotype score to identify elite trees for use in a next generation of tree breeding, as required in the claimed method of the invention.

For the reasons noted above, the cited references fail to teach, remotely suggest, provide any motivation to make, or otherwise render obvious the claimed invention. Accordingly, applicants respectfully request withdrawal of this ground of rejection.

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New Claims 21-28 depend from Claim 20 and further define the tree breeding method of the invention. They are supported throughout the specification, for example, at page 8, lines 30-35; page 9, lines 1-30; page 10, lines 7-16; page 12, lines 1-3; page 13, line 31, to page 14, line 2; page 16, line 19, to page 17, line 11; page 19, lines 30-35; and page 21, lines 23-32. No new matter has been introduced.

In view of the above amendments and the foregoing remarks, applicants respectfully submit that all the pending claims are in condition for allowance. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney.

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